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Commentary

BLOOD ACID-BASE BUFFERING: EXPLANATION OF THE EFFECTIVENESS OF BICARBONATE AND CITRATE INGESTION

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ABSTRACT

BLOOD ACID-BASE BUFFERING: EXPLANATION OF THE EFFECTIVENESS OF BICARBONATE AND CITRATE INGESTION. **Robert A. Robergs**. **JEPonline**. 2002;5(3):1-5. There exists confusion in the exercise and sports science community over the function and capacity of the bicarbonate (HCO_3^-) buffer system, as well as the mechanism of action of citrate ingestion for raising blood bicarbonate and pH. This commentary provides a brief explanation of buffers, and their mechanism of action. Blood buffers must function between a pH range of 7.2 to 7.4, while muscle intracellular buffers must function between pH values of 6.2 to 7.0. Ideally, the pK' characteristics of a buffer must be close to the pH of the tissue. However, the pK' values for carbonic acid (H_2CO_3) and HCO_3^- are 3.77 and 10.2, respectively. Despite these values, the bicarbonate system is a good blood buffer for pH values close to 7.4. This pK' and pH disparity results from the influence of body CO_2 stores on each of H_2CO_3 and HCO_3^-, effectively altering the pK' of the system close to 7.4. Increasing blood HCO_3^- increases the buffering capacity of blood, which in turn can improve intense intermittent exercise performance. Citrate does not have a pK' of an ionizable group that is effective within the range of blood pH. Nevertheless, citrate ingestion can increase blood HCO_3^- and pH. A review of the metabolic fate of citrate reveals that no protons are consumed in citrate catabolism. Thus, the benefit of citrate to blood buffering is based on its minor buffering capacity throughout the range of blood pH, and electrochemical properties that effectively raise blood HCO_3^- and pH though adjustments to the distributions of charged molecules within the intracellular and extracellular spaces. More research is needed for establishing the optimal mix of bicarbonate and citrate that most effectively improves blood proton buffering and intense exercise performance.

KEYWORDS: Acidosis, Protons, Carbonic acid, Citrate.

INTRODUCTION

Due to the confusion over the cellular biochemistry of metabolic acidosis (14), exercise physiologists are often questioned regarding the interpretation and application of this knowledge. This author has recently been

questioned on the buffering of acidosis, with particular emphasis on the role of bicarbonate. For example, there has been concern over the pK' of carbonic acid (3.77), and why citrate ingestion can increase the blood proton buffering capacity. This commentary provides explanation for why the pK' of carbonic acid (H_2CO_3) is so low, yet bicarbonate (HCO_3^-) (pK'=10.2) can function as the body's main blood buffer within the range of pH from 7.2 to 7.4. In addition, clarification is given for why citrate ingestion has a blood alkalizing effect.

THE BLOOD BICARBONATE BUFFERING SYSTEM

As previously explained (14), the pK' of an acid functional group refers to the pH at which half of the acid molecules are deprotonated (ionized). In other words, this is the pH when there is a dynamic equilibrium between the protons that leave and re-attach to the acid functional group of the molecule. Strong acids or acid functional groups have a pK' much lower than 7, and weak acids have pK' values closer to 7.0.

If you add molecules to the blood that are ionized and have a pK' close to 7.4 (±0.1 units), they will bind to protons and raise blood pH. The magnitude of the pH change will depend on the number of molecules that are added (molar strength), and the closeness of the pK' to a pH of 7.4. Consequently, for a buffer to be functional inside the body, it must be able to combine to a free proton at close to physiological pH. For cells, this pH is between 7.0 and 6.2, and for blood it is between 7.4 and 7.2. These ranges represent pH values from rest to intense exercise for both tissues, respectively.

Herein lies the confusion, if bicarbonate is the main blood buffer, and it readily binds to protons forming carbonic acid, how can this be true if the pK' for carbonic acid is so low (Table 1)? The low pK' of carbonic acid means that it could not be formed from a proton and bicarbonate unless the blood pH dropped to close to 3.8. This obviously does not occur in-vivo, yet bicarbonate is our main blood buffer.

Table 1. The pK' values for the bicarbonate buffer system components, and additional blood and cell buffers of protons close to physiological pH.

Proton Buffers	*Functional Group*	*pK'**
Dihydrogen phosphate ($H_2PO_4^-$)	NA	6.86
Acetic acid (CH_3COOH)	-COOH (carboxyl)	4.78
Carbonic acid (H_2CO_3)	NA	3.77
Bicarbonate (HCO_3^-)	NA	10.2
Bicarbonate system (H^+, HCO_3^-, H_2CO_3, CO_2, H_2O)	NA	~7.4#
Citrate (CH_2-COH-CH_2-(COOH)$_3$	-COOH (carboxyl)	3.15
	-COOH (carboxyl)	4.50
	-COOH (carboxyl)	5.75
Histidine ((COOH)CH(NH_3)CH_2C(NHCHN)CH)	-COOH (carboxyl)	1.8
	-side chain	6.0
	-NH^{3+} (amino)	9.2

*for 25°C ; #an estimate due to fluctuations in $PACO_2$, $PaCO_2$, and $CaCO_2$ (dissolved)
Lehninger et al. (6)

An often-cited biochemical depiction of the bicarbonate buffer system is presented below.

$$H^+ + Na^+HCO_3^- \Leftrightarrow H_2CO_3$$

The simple depiction above is very incomplete, and does not provide evidence for the discrepancy between pK' values for the components, and the functional buffering of the system close to a pH of 7.4 (Table 1). This discrepancy is explained by how the blood bicarbonate buffer system is not reliant on the acid-base qualities of bicarbonate and carbonic acid alone. The buffering power of the bicarbonate system is dependent on the

combined presence of bicarbonate, the enzyme carbonic anhydrase, and the body CO_2 stores (blood and lungs), as depicted below.

$$H^+ + Na^+HCO_3^- \Leftrightarrow H_2CO_3 \Leftrightarrow CO_2 + H_2O \Leftrightarrow CO_2$$

This more complex depiction of the bicarbonate buffer system reveals that there are now three reaction constants to consider;

$$K_1 = [H^+]\ [HCO_3^-] / [H_2CO_3]$$
$$K_2 = [H_2CO_3] / [CO_2d]\ [H_2O]$$
$$K_3 = [CO_2d] / [CO_2g]$$

where CO_2d=dissolved CO_2 and CO_2g = gaseous CO_2

Each of these constants needs to be computed into the new overall equilibrium constant that depicts the true buffering potential of this system. As explained by Lehninger (6), "*It [the bicarbonate buffer system] is unique,….. in that one of its components, carbonic anhydrase, is formed from dissolved carbon dioxide and water*." The three combined equilibrium constants raise the pK' of this system to close to 7.4, making it a very effective buffer against blood acidosis. It is unfortunate that the more complex acid-base biochemistry of this reaction is not mentioned in most textbooks of exercise physiology.

SUPPLEMENTING THE BLOOD AND MUSCLE BUFFERING SYSTEM

The differences between the pH of blood and muscle, and the unique qualities of the bicarbonate buffer system make supplementing the acid buffer potential of the body difficult. To increase the blood acid buffering capacity, you would need to either increase the capacity of the bicarbonate system (eg. ingest/infuse sodium bicarbonate), or add a molecule to the blood that has a pK' close to 7.4. To increase the muscle buffer capacity, you would need to add a molecule within the muscle cells that has a pK' close to 7.0. Alternatively, molecules could be added to the body that upon metabolism during exercise, consume a proton, thereby indirectly functioning as a buffer. I will discuss this option relative to the ingestion of sodium citrate later.

As the phosphate molecule has a terminal oxygen with a pK' close to 6.8, this is a very good cellular buffer (Figure 1). Histidine, an amino acid, is also a good cellular buffer due to the side chain pK' of 6.0 (Table 1). However, the blood buffer potential of phosphate and histidine are poor due to their relatively low blood concentrations. Sodium bicarbonate and sodium citrate (Figure 1) have been the two most researched options for increasing the blood buffering capacity. A wealth of research exists on the effectiveness of sodium bicarbonate ingestion to increase blood pH and buffering, and its influence on intense exercise performance (4,7,8). Research also shows the effectiveness of citrate ingestion on increasing blood pH and bicarbonate (1-3,9,11-13,16). However, compared to bicarbonate ingestion, intense exercise performance appears to be less improved following citrate ingestion. Given the pK' characteristics of citrate, why does it raise blood pH and bicarbonate?

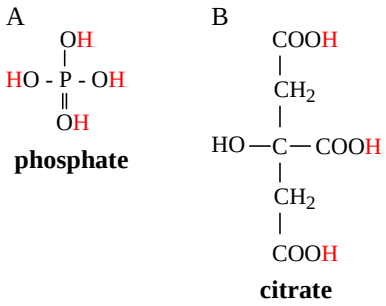

Figure 1. The chemical structures of a) phosphate and b) citrate. See Table 1 for the pK' characteristics of each molecule.

Citrate Ingestion and Proton Buffering

Citrate contains three carboxylic acid functional groups (Figure 1). However, at physiological pH, the relatively low pK' values of each functional group (Table 1) causes each to be completely ionized, resulting in a large negative ($^{-3}$) charge of citrate.

There are several proposed mechanisms for how citrate ingestion improves blood acid-base physiology. For example, proposed mechanisms for the increase in blood pH and HCO_3^- following citrate ingestion include;

1. blood and cellular proton buffering (11),
2. proton consumption during citrate oxidation in the TCA cycle (16),
3. bicarbonate production as a by-product of metabolism (12,16),
4. the negative charge of citrate increases the charge gradient between the blood and cells, causing protons to decease and HCO_3^- to increase (5), and
5. potentiation of the ATP inhibition of phosphofructokinase, causing a decrease in the rate of glycolysis and proton production (5).

Investigation of the catabolic pathway of citrate reveals that there is a net proton release during the TCA cycle (15), and therefore, no consumption of protons during citrate metabolism. In addition, there is no bicarbonate formed from citrate metabolism. As such citrate metabolism cannot contribute to a greater capacity to tolerate increased proton release. Consequently, the remaining mechanisms for the blood alkalizing effects of citrate ingestion are related to fundamental buffering, and/or the electrochemical explanation offered by Kowalchuk et al. (5). The latter electrochemical explanation is most consistent with the poor proton buffering qualities of citrate.

RECOMMENDATIONS

To rectify the misunderstandings of the bicarbonate buffer system, textbook and lecture explanations of this system need to stress the importance of CO_2 and how it modifies the pK' nature of the system compared to the pK' of the key components (HCO_3^- and H_2CO_3). In addition, the best explanation of the alkalizing effects of citrate ingestion appears to be its large negative charge, causing a decrease in blood protons and an increase in HCO_3^- to prevent disturbances in charge differences across cell membranes (5).

REFERENCES

1. Ball D, Maughan RJ. The effect of sodium citrate ingestion on the metabolic response to intense exercise following diet manipulation in man. ***Exp Physiol*** 1997;82(6):1041-56.
2. Cox G, Jenkins DG. The physiological and ventilatory responses to repeated 60 s sprints following sodium citrate ingestion. ***J Sports Sci*** 1994;12(5):469-75.
3. Hausswirth C, Bigard AX, Lepers R, Berthelot M, Guezennec CY. Sodium citrate ingestion and muscle performance in acute hypobaric hypoxia. ***Eur J Appl Physiol Occup Physiol*** 1995;71(4):362-8.
4. Horswill CA, Costill DL, Fink WJ, Flynn MG, Kirwan JP, Mitchell JB, Houmard JA. Influence of sodium bicarbonate on sprint performance: relationship to dosage. ***Med Sci Sports Exerc*** 1988;20(6):566-9.
5. Kowalchuk JM, Maltais SA, Yamaji K, Hughson RL. The effect of citrate loading on exercise performance, acid-base balance and metabolism. ***Eur J Appl Physiol Occup Physiol*** 1989;58(8):858-64.
6. Lehninger AB, Nelson DL, Cox MM (1993). Principles of biochemistry (second edition). New York, NY, Worth Publishers
7. Matson LG, Tran ZV. Effects of sodium bicarbonate ingestion on anaerobic performance: a meta-analytic review. ***Int J Sport Nutr*** 1993;3(1):2-28.
8. McNaughton L, Backx K, Palmer G, Strange N. Effects of chronic bicarbonate ingestion on the performance of high-intensity work. ***Eur J Appl Physiol Occup Physiol*** 1999;80(4):333-6.
9. McNaughton L, Cedaro R. Sodium citrate ingestion and its effects on maximal anaerobic exercise of different durations. ***Eur J Appl Physiol Occup Physiol*** 1992;64(1):36-41.
10. McNaughton L, Dalton B, Palmer G. Sodium bicarbonate can be used as an ergogenic aid in high-intensity, competitive cycle ergometry of 1 h duration. ***Eur J Appl Physiol Occup Physiol*** 1999;80(1):64-9.

11. McNaughton LR. Sodium citrate and anaerobic performance: implications of dosage. ***Eur J Appl Physiol Occup Physiol*** 1990;61(5-6):392-7.
12. Parry-Billings M, MacLaren DP. The effect of sodium bicarbonate and sodium citrate ingestion on anaerobic power during intermittent exercise. ***Eur J Appl Physiol Occup Physiol*** 1986;55(5):524-9.
13. Potteiger JA, Webster MJ, Nickel GL, Haub MD, Palmer RJ. The effects of buffer ingestion on metabolic factors related to distance running performance. ***Eur J Appl Physiol Occup Physiol*** 1996;72(4):365-71.
14. Robergs R.A. Exercise-induced metabolic acidosis: Where do the protons come from? ***Sportscience*** 2001 5(2), www.sportsci.org/jour/0102/rar.htm
15. Stryer L (1988). **Biochemistry** (third edition). New York, NY: W.H. Freeman
16. Tiryaki GR, Atterbom HA. The effects of sodium bicarbonate and sodium citrate on 600 m running time of trained females. ***J Sports Med Phys Fitness*** 1995;35(3):194-8.